SCN8A-related epilepsy with encephalopathy

SCN8A-related epilepsy with encephalopathy is a condition characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. The signs and symptoms of this condition typically begin in infancy.

The seizures in *SCN8A*-related epilepsy with encephalopathy include involuntary muscle contractions that occur before age 1 (infantile spasms), partial or complete loss of consciousness (absence seizures), involuntary muscle twitches (myoclonic seizures), or loss of consciousness with muscle rigidity and convulsions (tonic-clonic seizures). Most people with *SCN8A*-related epilepsy with encephalopathy have more than one type of seizure. The frequency of seizures in different individuals with this condition ranges from hundreds per day to fewer than one per month. In many individuals, the seizures are described as refractory because they do not respond to therapy with anti-epileptic medications.

Other signs and symptoms of *SCN8A*-related epilepsy with encephalopathy include intellectual disability that may be mild to severe. Some affected infants have normal early development but begin to lose previously acquired skills (developmental regression) and have a gradual loss in thinking ability (cognitive decline) when epilepsy develops. Problems with movement are common, and about half of affected infants cannot perform intentional movements. Behavior disorders may also occur.

In rare cases, individuals with this condition die unexpectedly for no known reason (sudden unexpected death in epilepsy or SUDEP).

Frequency

There are at least 140 individuals with *SCN8A*-related epilepsy with encephalopathy. This condition is estimated to account for 1 percent of all cases of epilepsy with encephalopathy.

Causes

As its name suggests, *SCN8A*-related epilepsy with encephalopathy is caused by mutations in the *SCN8A* gene. This gene provides instructions for making one part (the alpha subunit) of a sodium channel called $Na_v1.6$. This channel allows positively charged sodium (Na) atoms (sodium ions) to pass into nerve cells (neurons) and plays a key role in the ability of neurons to communicate by generating and transmitting electrical signals.

SCN8A gene mutations result in altered $Na_v1.6$ channels that stay open longer than usual, which increases the flow of sodium ions into neurons. The persistently open channels abnormally increase electrical signals, which can lead to excess activation

(excitation) of neurons in the brain. The increased neuronal activity leads to seizures in people with *SCN8A*-related epilepsy with encephalopathy.

It is unknown how *SCN8A* gene mutations lead to intellectual disability, movement problems, and the other features of *SCN8A*-related epilepsy with encephalopathy. Because some affected children experience developmental regression after the onset of seizures, it has been suggested that the seizures may impair brain function, but it is unclear if that is the case.

Inheritance Pattern

This condition follows an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- early infantile epileptic encephalopathy 13
- EIEE13
- SCN8A encephalopathy

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Early infantile epileptic encephalopathy 13
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3281191/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22SCN8A-related+epilepsy+with+encephalopathy%22+OR+%22early+infantile+epileptic+encephalopathy+13%22+OR+%22early+infantile+epileptic+encephalopathy%22

Other Diagnosis and Management Resources

- GeneReview: SCN8A-Related Epilepsy with Encephalopathy
  https://www.ncbi.nlm.nih.gov/books/NBK379665

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html

Genetic and Rare Diseases Information Center

- SCN8A encephalopathy
  https://rarediseases.info.nih.gov/diseases/13085/scn8a-encephalopathy

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Encephalopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page
- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page

Educational Resources

- Boston Children's Hospital: Epilepsy and Seizure Disorder in Children
  https://www.childrenshospital.org/Conditions-and-Treatments/Conditions/E/Epilepsy
- Centers for Disease Control and Prevention: Epilepsy
  https://www.cdc.gov/epilepsy/index.html
- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html
- MalaCards: scn8a-related epilepsy with encephalopathy
  https://www.malacards.org/card/scn8a_related_epilepsy_with_encephalopathy
- Merck Manual Consumer Version: Seizure Disorders
  https://www.merckmanuals.com/home/brain,-spinal-cord,-and-nerve-disorders/seizure-disorders/seizure-disorders
- Orphanet: Early infantile epileptic encephalopathy
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1934

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/
- American Epilepsy Society
  https://www.aesnet.org/

- CURE: Citizens United for Research in Epilepsy
  https://www.cureepilepsy.org/
- Epilepsy Canada
  https://www.epilepsy.ca/
- Epilepsy Society (UK)
  https://www.epilepsysociety.org.uk/
- Medical Home Portal: Seizures/Epilepsy
  https://www.medicalhomeportal.org/diagnoses-and-conditions/seizures-epilepsy
- SCN8A.net from The University of Arizona
  https://scn8a.net/
- The Cute Syndrome Foundation
  https://www.thecutesyndrome.com/

Clinical Information from GeneReviews

- SCN8A-Related Epilepsy with Encephalopathy
  https://www.ncbi.nlm.nih.gov/books/NBK379665

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SCN8A-related+epilepsy+with+encephalopathy%5BTIAB%5D%29+OR+%28SCN8A+encephalopathy%5BTIAB%5D%29+OR+%28early+infantile+epileptic+encephalopathy+13%5BTIAB%5D%29+OR+%28SCN8A%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 13
  http://omim.org/entry/614558

Medical Genetics Database from MedGen

- Early infantile epileptic encephalopathy 13
  https://www.ncbi.nlm.nih.gov/medgen/482821

Sources for This Summary

- Butler KM, da Silva C, Shafir Y, Weisfeld-Adams JD, Alexander JJ, Hegde M, Escayg A. De novo and inherited SCN8A epilepsy mutations detected by gene panel analysis. Epilepsy Res. 2017 Jan; 129:17-25. doi: 10.1016/j.eplepsyres.2016.11.002. Epub 2016 Nov 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27875746
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5321682/
- Hammer MF, Wagnon JL, Mefford HC, Meisler MH. SCN8A-Related Epilepsy with Encephalopathy. 2016 Aug 25. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK379665/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27559564
- Larsen J, Carvill GL, Gardella E, Kluger G, Schmiedel G, Barisic N, Depienne C, Brilstra E, Mang Y, Nielsen JE, Kirkpatrick M, Goudie D, Goldman R, Jähn JA, Jepsen B, Gill D, Döcker M, Biskup S, McMahon JM, Koeleman B, Harris M, Braun K, de Kovel CG, Marini C, Specchio N, Djémié T, Weckhuysen S, Tommerup N, Troncoso M, Troncoso L, Bevot A, Wolff M, Hjalgrim H, Guerrini R, Scheffer IE, Mefford HC, Møller RS; EuroEPINOMICS RES Consortium CRP. The phenotypic spectrum of SCN8A encephalopathy. Neurology. 2015 Feb 3;84(5):480-9. doi: 10.1212/WNL.0000000000001211. Epub 2015 Jan 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25568300
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4336074/
- Meisler MH, Helman G, Hammer MF, Fureman BE, Gaillard WD, Goldin AL, Hirose S, Ishii A, Kroner BL, Lossin C, Mefford HC, Parent JM, Patel M, Schreiber J, Stewart R, Whittemore V, Wilcox K, Wagnon JL, Pearl PL, Vanderver A, Scheffer IE. SCN8A encephalopathy: Research progress and prospects. Epilepsia. 2016 Jul;57(7):1027-35. doi: 10.1111/epi.13422. Epub 2016 Jun 8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27270488
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5495462/
- Wagnon JL, Barker BS, Hounshell JA, Haaxma CA, Shealy A, Moss T, Parikh S, Messer RD, Patel MK, Meisler MH. Pathogenic mechanism of recurrent mutations of SCN8A in epileptic encephalopathy. Ann Clin Transl Neurol. 2015 Dec 21;3(2):114-23. doi: 10.1002/acn3.276. eCollection 2016 Feb.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26900580
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4748308/

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https://ghr.nlm.nih.gov/condition/scn8a-related-epilepsy-with-encephalopathy

Reviewed: August 2017
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
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